Tetrahedron Letters No.7, pp. 479-480, 1970. Pergamon Press. Printed in Great Britain.

PYRAZOLES VII: NITRATION OF 1,4-DISUBSTITUTED PYRAZOLES (1)

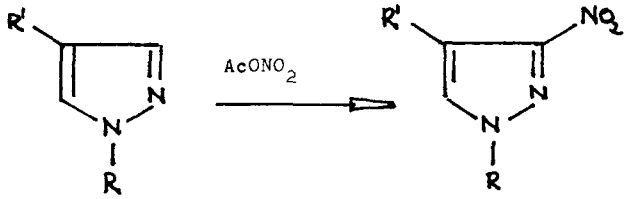
Clarisse L.Habraken, Pauline Cohen-Fernandes, S.Balian (2) and K.C.van Erk (2)

Laboratory of Organic Chemistry, The University, P.O.Box 75, Leiden, The Netherlands

(Received in UK 11 December 1969; accepted for publication 8 January 1970)

Nitration of pyrazoles is generally considered to occur only at the 4-position (3). Recently, however, the successful nitration of the pyrazole nucleus of 4-picrylamino- and 4-phenylpyrazoles (4,5) has been reported.

In an investigation on the nitration of pyrazoles IA, IIA and IIIA with acetyl nitrate, at 0°, we have obtained the corresponding 3-nitropyrazoles IB, m.p.97°, PMR δ 2.35 (s,3), 4.01 (s,3) and 7.40 (s,1); IIB, m.p. 103°, PMR δ 1.30 (t,3), 2.96 (q,2), 4.30 (s,3) and 7.70 (s,1); and IIIB, m.p. 79°, PMR δ 1.30 (t,3), 2.91 (q,2), aromatic protons 7.66 - 8.25 (6) as the main products of the reaction (6,7).



IA, IIA, IIIA IB, IIB, IIIB

I R=R'=CH_3

II R=CH_3; R'=C_2H_5

III R=C_6H_5; R'=C_2H_5

Oxidation of the 4-alkyl group in IB and IIB afforded the identical nitro substituted 1-methyl-4-pyrazole carboxylic acid IV, m.p. 179-180°, IR 5.71 (C=O) and 6.48 and 7.40 (NO_2). A comparison of IV with an authentic sample of 1-methyl-5-nitro-4-pyrazole carboxylic acid (8) (IR spectrum, TLC and mixed melting point) showed that the two products were non-identical. IV has been, consequently, assigned the structure 1-methyl-3-nitro-4-pyrazole carboxylic acid. It follows as a corollary that the nitro group in IB and IIB must occupy, in each case, the 3-position of the pyrazole ring.

IIIB exhibits a multiplet for the phenyl protons. Such a multiplet is only found for

phenylpyrazoles which are unsubstituted in positions α to the phenyl substituent; in α - substituted phenylpyrazoles, on the contrary, the phenyl protons show up essentially as a singlet (9). In addition, the downfield shift of the 4-ethyl methylene protons in IIIB - as compared to IIIA - is of the same magnitude as is found for the analogous protons in IB and IIB.

These findings lead us to the conclusion that, under suitable conditions, the pyrazole ring is quite susceptible to electrophilic substitution at positions other than the, till hitherto favoured, C_4-position.

References

(1) Part VI: C.Winberger and C.L.Habraken, J.Heterocyclic Chem., 6, 545 (1969).

(2) Participant in the "Undergraduate Research Project Program", summer 1969, supported by "Pieter Langerhuizen Lzn. Fonds", administered by "De Hollandsche Maatschappij der Wetenschappen".

(3) A.R.Katritzky and J.M.Lagowski, "The Principles of Heterocyclic Chemistry", Methuen and Co. Ltd., London 1967, p. 148.

(4) M.D.Coburn, 2nd International Congress Of Heterocyclic Chemistry, Montpellier, France 1969; ibid., J.Heterocyclic Chem., in press.

(5) P.Cohen-Fernandes and C.L.Habraken, 2nd International Congress of Heterocyclic Chemistry, Montpellier, France, 1969; ibid., to be published.

(6) All new compounds gave satisfactory elemental analyses; PMR spectra were recorded in $CDCl_3$ solution with TMS as internal standard; IR spectra were taken in KBr disk.

(7) Currently we are investigating the other reaction products of the nitration of 4-ethyl-1-phenylpyrazole; among these products, we could not detect, either 4-ethyl-1-(p-nitrophenyl) pyrazole or 4-ethyl-1-(o,p-dinitrophenyl) pyrazole.

(8) C.C.Cheng, J.Heterocyclic Chem., 5, 195 (1968); we thank Dr. C.C.Cheng for providing us this sample.

(9) L.G.Tensmeyer and C.Ainsworth, J.Org.Chem., 31, 1878 (1966).